¹ Reducing antimicrobial use on dairy farms

² using a herd health approach

3 Robert Hyde, David Tisdall, Paddy Gordon, John Remnant

4 Introduction

5 Antimicrobial use (AMU) and antimicrobial resistance (AMR) have received a great deal of media 6 attention, and with the government commissioned O'Neill report calling for a reduction of 7 unnecessary AMU in agriculture (O'Neill 2015), there is a high level of scrutiny of the livestock 8 industry. Concerns exist that increased AMU in cattle might increase the prevalence of resistant 9 pathogens (Saini et al., 2013), and although the importance of agricultural AMU in AMR risk to the 10 human population is largely unknown (Tang et al., 2017), the potential "One Health" consequences 11 of inappropriate AMU to both human and animal health means current and future AMU levels 12 within the dairy industry require careful consideration. Dairy "herd health" is an approach to the 13 veterinary care of dairy cattle applied at a population level, rather than the individual animal level 14 (Green 2012). The focus of herd health is on preventing disease in the herd, often using a data driven 15 approach. It follows that providing effective herd health advice to dairy farms alongside continuous 16 monitoring and analysis has huge potential to reduce AMU on farm, by preventing disease, and 17 therefore avoiding the need for antimicrobials. This herd health approach should also improve 18 animal welfare, reduce cost to the farmer, and increase production - making reductions in AMU 19 achieved by this route very sustainable. This article outlines key herd health approaches to common 20 diseases on dairy farms that will result in a decrease in AMU, with a focus on those interventions 21 most likely to result in the biggest reductions.

22 Measuring antimicrobial use

Monitoring and benchmarking AMU has been identified as an important intervention to incentivise
reduced AMU in livestock (Speksnijder *et al.*, 2015), and farm assurance schemes now often include

- 25 an antimicrobial monitoring component (i.e. Red Tractor Farm Assurance). Much as clinical disease
- 26 levels and economic outcomes are commonly calculated to assess the impact of herd health
- 27 interventions, the reduction of AMU can also provide a straightforward, objective measurement of a
- 28 key outcome of interest for UK dairy farms (see Figure 1). The freely available University of
- 29 Nottingham AMU Calculator and Benchmarking Tool provides a simple platform for both
- 30 veterinarians and farmers to assess AMU by both dose and mass based methodologies, as well as
- 31 providing analysis of groups of farms (Hyde *et al.*, 2017) (see Figure 2). A summary of approaches to
- 32 measuring AMU is provided in Box 1. The Responsible Use of Medicines in Agriculture Alliance
- 33 (RUMA) targets task force have created a series of targets for the UK dairy industry using standard
- 34 European Medicines Agency metrics (RUMA 2017), as described in
- 35 Table 1 The RUMA Target Task Force dairy sector targets compared with the most recent dairy
- 36 antimicrobial usage (AMU) figures from~31% of the national dairy herd (VARRS 2017).

	Subject	Current dairy AMU (VARRS 2017)		RUMA Target (2020)
1	HP-CIA injectables (mg/PCU)		0.76	0.54
2	HP-CIA intra-mammary use (DCDVet)		0.22	0.17
3	Intra-mammary tubes – dry cow (DCDVet)		0.68	0.67
4	Intra-mammary tubes – lactating cow (DCDVet)		0.82	0.73
5	Sealant tube usage (average number of courses per dair	y cow)		0.70
6	Total antimicrobial usage (mg/PCU)		17	21

HP-CIA: Highest Priority critically important antimicrobials, mg/PCU: milligrams of antimicrobials used per population correction unit, DDDvet: defined daily dose, DCDvet: defined course dose

- 37 , and there is continued involvement in this area from organisations such as the Veterinary
- 38 Medicines Directorate (VMD) and the Cattle Health and Welfare Group (CHAWG).

Table 1 The RUMA Target Task Force dairy sector targets compared with the most recent dairy antimicrobial usage (AMU)
 figures from~31% of the national dairy herd (VARRS 2017).

	Subject	Current dairy AMU (VARRS 2017)	RUMA Target (2020)
1	HP-CIA injectables (mg/PCU)	0.76	0.54
2	HP-CIA intra-mammary use (DCDVet)	0.22	0.17
3	Intra-mammary tubes – dry cow (DCDVet)	0.68	0.67
4	Intra-mammary tubes – lactating cow (DCDVet)	0.82	0.73
5	Sealant tube usage (average number of courses per dair	y cow)	0.70
6	Total antimicrobial usage (mg/PCU)	17	21

HP-CIA: Highest Priority critically important antimicrobials, mg/PCU: milligrams of antimicrobials used per population correction unit, DDDvet: defined daily dose, DCDvet: defined course dose

Measurements of antimicrobial use

European medicines agency metrics

mg/PCU = Milligrams of antimicrobial used per population correction unit

DDDvet = Defined daily dose for animals

DCDvet = Defined course dose for animals

AMU can broadly be measured in two ways; by mass- or dose-based methodology. Mass-based methodologies measure the milligrams (mg) of antimicrobial used on a farm, per kg of animal at time of treatment; population correction unit (PCU). Dose based methodologies estimate the number of doses or courses of antimicrobial each animal receives, with injectable antimicrobials being assigned a standard dosage (i.e. Amoxicillin; 8mg/kg), and single treatments such as intramammary tubes counting as a single dose, regardless of mg. Detailed, farm level AMU in British dairy farms have recently been reported (Hyde *et al.*, 2017) with injectable, footbath and oral antimicrobial use being shown to be strong drivers of AMU measured by mg/PCU, and intramammary treatments strong drivers of AMU measured by DDDvet and DCDvet. It is worth noting that topical antimicrobials such as sprays are not included in ESVAC metrics, and whilst dry cow therapy is included in DCDvet and mg/PCU metrics, it is not included in the calculation of DDDvet. One particular point to note when calculating AMU via ESVAC methodology is the use of the 425kg adult dairy cow weight, which has the potential to confuse producers if not explained that this is intended to represent the average weight at time of treatment rather than the actual weight of an adult cow.

Whilst there has been some debate as to which metrics are likely to be most appropriate for the UK situation, there is currently no clear evidence as to which metrics are optimal for recording AMU, and ultimately incentivising reductions in both AMU and AMR. As the veterinarian analysing dairy herd mastitis will employ both SCC and clinical mastitis cases to inform herd level mastitis control decisions, it would appear prudent to apply a combination of both dose and mass-based methodologies when analysing AMU on farms.

A detailed review evaluating metrics available for benchmarking AMU in the dairy industry is available from Mills *et al.*, (2018).

42

43 Motivating change

44 The motivations for the use of antimicrobials are complex for both veterinarian and farmer, and the

45 decision to administer or prescribe can be influenced by a range of often competing intrinsic and

46 extrinsic factors. Intrinsic factors exert a powerful influence on behaviour. Experience, confidence,

47 attitude to risk and uncertainty all influence an individuals' tendency to administer or prescribe, and 48 in human medicine, these factors have been found to be some of the biggest determinants of 49 antimicrobial prescribing rate (De Sutter et al., 2001). It would be unsurprising to find that the same was true in the farm animal context, where individual treatment decisions are often made by the 50 51 farmer in the absence of direct veterinary supervision, and poor compliance with treatment 52 protocols is common from a UK perspective (Sawant et al., 2005). There are also a range of extrinsic factors, including the clinical presentation, patient characteristics, economics and withhold times. 53 54 Add to this the tendency of antimicrobial users towards defensive prescribing; the "precautionary 55 principle", encapsulated by the idea of administering antimicrobials "just in case", and the pressure 56 towards inappropriate use becomes clear. In spite of this, there is clear evidence of motivation 57 amongst dairy farmers to reduce AMU, and it has also been shown that farmers consider veterinary 58 surgeons to be the most influential source of information in this regard (Jones et al., 2015). It is 59 important to acknowledge this complexity when designing any strategy to motivate change in AMU 60 on farm and to recognise the need to equip veterinary surgeons with appropriate communication skills training (e.g. motivational interviewing) (Bard et al., 2017; van Dijk et al., 2017) 61 62 Proactive, multi-disciplinary, collaborative approaches from veterinarians to improve animal health 63 alongside targeted reductions of the use of highest priority critically important antimicrobials (HP-CIAs, which include 3rd and 4th generation cephalosporins, fluoroquinolones and colistin) have been 64 65 shown to be effective, without significant effect on animal health outcomes (Tisdall et al., 2016; Turner et al., 2018). When farmers are drawn in as partners in the process and the competing 66 factors which influence motivation are addressed, revisions in AMU policy as part of a proactive 67 68 approach to herd health management becomes routine, and real behavioural change can occur. 69 Farmer training on compliance and responsible use (such as the avoidance of HP-CIAs) is important, 70 but information alone is insufficient to produce lasting behavioural change. The importance of 71 intentional, one-to-one conversations with veterinary surgeons who are modelling best-practice,

- 72 alongside the powerful influence of changing social norms and farmer role models should not be
- vnderestimated.

74 Herd Health

- 75 A summary of the key areas of dairy cow herd health that can lead to AMU reduction follows. A
- summary of key interventions for each area is provided in Box 2 and the potential impact in Figure 3.

Box 2 A summary of the key interventions to reduce inappropriate AMU on dairy farms using a herd health approach

The following list summarises some key steps in dairy herd health that are likely to reduce inappropriate AMU on dairy farms

- Udder health
 - Reduction in clinical mastitis incidence by implementing, for example, the AHDB dairy mastitis control plan
 - Cease use of injectable antimicrobial mastitis therapy as an adjunct to intra-mammary therapy and use NSAIDs instead
 - Implement selective dry cow therapy to reduce AMU and reduce Gram negative mastitis cases post-calving
 - Consider if on farm culture could be appropriate (e.g. low levels of Gram positive mastitis, and only if considering not treating Gram negative cases, which may not be economically worthwhile)
- Lameness
 - Eliminate the use of antibiotic footbaths
 - o Identify lameness prevalence and predominant lesion(s)
 - Ensure early detection and treatment
 - o Treat claw horn disease with NSAIDs and block, not antimicrobials
 - o Implement effective prevention strategies (e.g. improve cubicle comfort, improve hygiene)
- Reproductive health
 - Monitor calving health, disease incidence, energy balance and levels of hypocalcaemia in order to effectively implement control strategies if above target levels.
 - o Optimise transition cow nutrition, housing and management
 - Eliminate use of highest priority critically important antimicrobials (HP-CIAs) e.g. Ceftiofur
- Youngstock
 - Monitor and ensure adequate passive transfer/colostrum intake
 - Optimise environmental conditions (e.g. bedding hygiene, ventilation) and nutrition
 - Avoid the use of antimicrobials in the treatment of calf diarrhoea, in the absence of clinical signs consistent with septicaemia and culture and sensitivity testing
 - o Consider respiratory disease vaccination if appropriate
 - Eliminate the use of in-milk antimicrobials for prophylaxis/metaphylaxis
- Infectious disease
 - o Ascertain current disease status and implement appropriate biosecurity
 - Join or align with national initiatives (i.e. BVD eradication) where appropriate
 - Use vaccination to help control endemic disease when required (BVD, respiratory disease etc)

77 Udder health

Mastitis remains one of the greatest challenges to the UK dairy industry (Bradley 2002), and can
significantly affect AMU; being responsible for up to 68% of AMU when measured by dose based
methodology (Kuipers *et al.*, 2016). 4 out of the 6 RUMA dairy sector targets relate directly to
mastitis therapy (Table 1), and by reducing both clinical mastitis and antimicrobial dry cow therapy a
significant reduction in dairy farm AMU can be achieved (Kromker and Leimbach 2017).

83 One method of mastitis reduction with a strong evidence base is the implementation of the AHDB 84 Dairy Mastitis Control Plan (DMCP: www.dairy.ahdb.org.uk/technical-services/mastitis-control-plan), 85 with plan users being shown to achieve a 20 percent reduction in clinical mastitis incidence 86 compared with control farms (Green et al., 2007). Recent data suggests a 40 percent decrease in 87 lactating cow intra-mammary AMU achieved via use of the DMCP (Bradley et al., 2017, Breen et al., 88 2017) (Box 3). Generally unnecessary additional treatments such as the use of parenteral 89 antimicrobials have no beneficial effects on the outcomes of mild/moderate clinical mastitis (Wenz et al., 2005), and the use of systemic antimicrobials can contribute to high AMU (mg/PCU) on dairy 90 91 farms (Hyde et al., 2017). In contrast, the use of non-steroidal anti-inflammatory medication 92 (NSAIDs) have clear benefits in the treatment of clinical mastitis and should be encouraged (Leslie 93 and Petersson-Wolfe 2012). Gram negative mastitis may cure spontaneously without the use of 94 antimicrobials, and as a result, interest in the use of on-farm culture systems to target treatment is 95 increasing (Lago et al., 2011). Culture of mild clinical cases prior to antimicrobial treatment allows 96 determination of bacterial cause avoiding unnecessary treatment. Caution is urged however, as due 97 to decreased cure rates associated with delaying treatment of gram positive cases, this may not be 98 cost effective for all UK farms (Down et al., 2017). The blanket use of antimicrobial dry cow therapy 99 (DCT) regardless of infection status is challenging to justify, and selective DCT using recent somatic 100 cell count and clinical mastitis data (for example having a somatic cell count <200,000 cells/ml and 101 no clinical mastitis within the last 3 individual monthly recordings (Bradley et al., 2010)) can 102 dramatically reduce AMU when measuring DCDvet. In addition, the use of selective DCT has been

103	found to decrease prevalence of <i>E.coli</i> clinical mastitis cases post-calving (Bradley <i>et al.,</i> 2010)
104	compared with antimicrobial DCT, resulting in a potential reduction in disease incidence alongside a

reduction in AMU.

- 106 With a primary focus on the reduction of clinical mastitis incidence through the implementation of
- 107 the DMCP, the reduction in generally unnecessary treatments such as parenteral therapy of
- 108 mild/moderate cases, and adoption of selective DCT, it should be possible to dramatically reduce
- 109 mastitis related AMU. It is worth noting reductions in intramammary usage primarily impacts dose or
- 110 course based measures (rather than mass) as intra-mammary preparations typically have lower
- amounts of antimicrobial compared to systemic treatments. The role of the farm animal veterinarian
- 112 must extend far beyond the treatment of individual cases of mastitis, and epidemiological data
- analysis skills in determining mastitis origin at herd level are likely to be extremely important in
- implementing effective mastitis control measures (Green et al., 2007).

Box 3. Example reductions in AMU through implementation of the AHDB Dairy Mastitis Control Plan

The implementation of the AHDB Dairy Mastitis Control Plan on a 600 cow dairy farm has been described as a case report (Breen et al., 2017), highlighting a reduction of clinical mastitis cases from a rate of 60-70 cases per 100 cows/year to less than 20 cases per 100 cows/year. Following analysis of herd level clinical mastitis and somatic cell count data, a focus on dry cow cubicle management as well as drying off technique resulted in dramatic reductions in both clinical and subclinical mastitis. This was paired with a reduction in AMU from 40mg/PCU and 14 DDDvet to 26mg/PCU and 7 DDDvet over a 3-year period, highlighting the positive impact that herd level interventions can have on both animal health and welfare whilst simultaneously reducing AMU.

115

116 Lameness

- 117 Lameness is a common presentation in dairy cattle and significant cause of financial loss and poor
- 118 welfare. The most common causes of lameness are conditions of the foot, and these can be divided
- 119 into claw horn lesions (sole haemorrhage/sole ulcer and white line disease) and soft tissue infections
- 120 (interdigital phlegmon and digital dermatitis) (Archer et al., 2010). Investigations of lameness at a

herd level should aim to establish prevalence (for example by mobility scoring) and the predominant
lesion types present on the farm by examining the feet of lame cows and analysing foot trimming
records.

124 A discussion of the causes of claw horn lesions is beyond the scope of this article, and has been 125 undertaken elsewhere (Mahendran and Bell, 2015). However, it is clear bacterial infection is not 126 thought to play a role in the pathogenesis (Newsome *et al.,* 2016). It should not be necessary to 127 treat claw horn lesions with antimicrobials and the best outcomes for the treatment of claw horn 128 disease are achieved with the application of a foot block and the administration of a NSAID (Thomas 129 et al., 2015). When detection and treatment are delayed, cure rates decline (Thomas et al., 2016), 130 and regular mobility scoring has been described as an effective way of identifying early cases 131 (Groenevelt et al., 2014). As well as better outcomes for the cows, early and effective treatment 132 should prevent cases progressing to deep digital sepsis and other complications where 133 antimicrobials would be required. Lame cows should not be given injectable antimicrobials as an 134 alternative to examination of the foot. Prevention of the lesions should focus on improving lying 135 comfort, reducing standing times, and reducing potential trauma (inappropriately sharp turns and 136 high stocking rates), and regular foot trimming to quickly treat cows that do become lame.

137 Soft tissue lameness is more likely to be bacterial in origin with interdigital phlegmon (foul) caused 138 by Fusobacterium necrophorum and other bacteria and digital dermatitis thought to be caused by 139 Treponema species (Maxwell et al., 2015). Clearly in these cases antimicrobial treatment may be 140 justified, although only topical treatment is required for most digital dermatitis lesions (Laven and 141 Logue 2006). Cure rates remain low with common topical and systemic treatments and improved 142 antimicrobial or non-antimicrobial treatment protocols are required and may be developed (Evans et 143 al., 2016). Prevention should focus on improving environmental hygiene and in particular underfoot 144 conditions. Regular use of a disinfectant foot bath is an essential measure in the control of digital 145 dermatitis with evidence to support the use of both formalin and copper sulphate products (Bell et

146 al., 2014). Care needs to be taken with either product, formalin is a carcinogen and alongside 147 concerns of environmental accumulation there is evidence that heavy metals such as copper may 148 select for AMR (Hobman & Crossman, 2018). Anecdotally, some herds have used antibiotic footbaths 149 to control digital dermatitis. This practice is associated with extremely high levels of AMU, with 150 farms using antibiotic footbaths being far more likely to be "high users" overall (Hyde et al., 2017) 151 and is no longer considered acceptable or necessary (Bell et al., 2017). Where the prevalence of acute digital dermatitis is high and/or disinfectant footbaths would cause too much discomfort to 152 153 affected cows then targeted topical treatment (for example the application of oxytetracycline spray) 154 of individual animals should be carried out, resulting in a significantly decreased level of AMU 155 compared with herd level antibiotic footbathing.

156 Reproduction

157 Postpartum reproductive disease is relatively common in dairy cows, and the combination of 158 reduced fertility, increased risk of culling, and increased AMU associated with these conditions 159 makes their control and prevention extremely important (Gilbert 2016). The treatment of 160 postpartum diseases such as metritis have historically involved the use of ceftiofur, however the use 161 of HP-CIAs essential for human medicine largely on the basis of zero milk withdrawal is extremely 162 difficult to defend. Many alternatives to HP-CIAs exist, and these should be considered wherever 163 possible, particularly in light of recent farm assurance changes such as the Red Tractor antibiotic 164 standards. Practitioners should be aware that the swapping of HP-CIAs to non-critical alternatives 165 may result in an increase in overall AMU as measured by mass based methodologies, due to the 166 relatively low dosing requirements of HP-CIAs (i.e. ceftiofur dosage: 1mg/kg, amoxicillin: 8mg/kg). 167 Also to be considered are bulk tank residue failures if farmers' are not adequately informed of milk 168 withdrawal requirements of HP-CIA alternatives, as well as the significant risks posed by the feeding 169 of antimicrobial waste milk to calves as a route of disposal (Ricci et al., 2017). Treatment of bacterial 170 reproductive disease such as metritis with antimicrobials can be justified, however cases of retained 171 fetal membranes should not need antimicrobial treatment in the absence of pyrexia (Drillich et al.,

2006). Whilst the treatment of clinical endometritis with intrauterine cephapirin has been shown in
several studies to improve reproductive outcomes (Hyde & Brennan, 2017), the use of antimicrobial
treatments for reasons other than cow health may be challenging to justify. Alternatives to
antimicrobials such as prostaglandin treatments are widely used, although their efficacy in improving
reproductive outcomes have been called into question (Haimerl *et al.*, 2013). It is far more effective
to prevent diseases such as endometritis than rely on treatment options with limited evidence of
efficacy.

179 The prevention of postpartum reproductive disease focusses on maintaining dry matter intake over 180 the dry period, reducing negative energy balance and improving hygiene (Gilbert 2016), as well as 181 minimising social group changes . A diagnostic approach to transition cow disease should focus on 182 housing, management and nutrition. Key aspects are ensuring adequate feed space, ration 183 composition and stocking density to maximise feed intake as well as control of hypocalcaemia and 184 negative energy balance, all of which are areas practitioners can regularly monitor. A minimum feed 185 space of 76cm per cow has been recommended for transition cows (Cook and Nordlund 2004), with 186 a minimum required area per cow of 1.25m²/1,000 litres/year (Green *et al.*, 2007) in loose housing. 187 Cows should be assessed for body condition, lameness and infectious disease. Consideration can be 188 given to the use of preventive treatments, such as a monensin (although it is worth noting monensin 189 is also an antibiotic) or immune restoratives (Ruiz et al., 2017), although recent studies suggest the 190 potential for immune restorative products such as pegbovigrastim to have significant detriment to 191 cow health (Zinicola et al., 2018).

Both pre-partum energy balance monitoring with non-esterified fatty acid (NEFA) testing, and postpartum with beta-hydroxybutyrate (BHB) testing as a herd level strategy to identify both individual and herd level issues is of value (Ospina *et al.*, 2013). For example, early identification of ketotic cows via BHB testing and subsequent treatment with propylene glycol might prevent downstream complications of ketosis such as metritis and left-displacement of the abomasum (LDAs). 197 Furthermore, the regular monitoring of these metabolites at a herd level can be invaluable in

determining where attention best be focused to prevent post-partum reproductive disease.

199 Youngstock

200 Neonatal calf diarrhoea and bovine respiratory disease (BRD) are common causes of morbidity and 201 mortality in calves, and both are frequently treated with antimicrobials. Whilst calf AMU often has a 202 relatively minor effect on overall herd AMU figures, these diseases represent a significant cost both 203 in terms of economics and welfare, and remain a great opportunity for AMU reduction relative to 204 calves. Treatment decisions are complicated by mixed viral, bacterial and protozoal aetiologies, and 205 patterns of clinical signs which lack specificity for each cause. In addition, a wide range of risk factors 206 relating to the housing environment and husbandry practices are at play. The combination of 207 uncertainty surrounding a specific diagnosis, the relatively low cost and practical simplicity of 208 antimicrobial therapy, and an aversion to risk, potentially all contribute to defensive prescribing in 209 these cases.

210 The use of calf-side diagnostics can help predominant pathogen identification in cases of calf 211 diarrhoea, though mixed infections are commonly present. Control should focus on maximising calf 212 immunity through effective passive transfer of colostral immunity and reducing the pathogen 213 challenge by improving environmental hygiene (Lorenz et al., 2011). Therapy should focus on fluid 214 rehydration by oral or intravenous routes, dependant on the degree of shock (Meganck et al., 2014). 215 NSAIDs are also appropriate, where adequate renal perfusion is maintained. Antimicrobial therapy 216 of neonatal calf diarrhoea with oral boluses or parenteral injections are not needed, with the 217 exception of severely sick animals, for example those affected with septicaemia associated with E. 218 coli in the first few days of life (Constable 2004).

Control of BRD should again focus on achieving adequate passive transfer as well as improving
 environmental conditions and nutrition (for example improved ventilation, increased frequency of
 bedding and adequate energy intake) (Gorden and Plummer 2010). In closed herds identifying the

222 causative primary pathogens may be of value to inform preventive strategies. Sampling of acute 223 cases of respiratory disease using broncho-alveolar lavage (BAL), trans-tracheal washes and 224 conjunctival/nasopharyngeal swabs are techniques underused in clinical practice to inform 225 treatment decisions. Culture and sensitivity results from post-mortem submissions may have more 226 limited value in informing treatment decisions because they often represent chronic cases and 227 treatment failures rather than the primary agent, however post-mortem examination can be 228 extremely valuable when cases are appropriately selected. Retrospective or ideally paired serology 229 of cohorts undergoing the same management system can be useful to identify predominant 230 pathogens, but has less value therapeutically. An extensive range of vaccines are available for the 231 common causes of respiratory disease, although are unlikely to completely prevent disease in the 232 presence of poor environmental conditions (Sherwin and Down 2018). Similarly, vaccination of dams 233 to provide immunity to calves for the causative agents of diarrhoea will not be effective if colostrum 234 and environmental management is inadequate.

235 Prophylactic use of antimicrobials should be avoided, with a clear emphasis placed on preventing 236 disease. The use of tetracyclines to medicate milk powder as a control strategy for BRD does not 237 represent responsible AMU (VMD, 2013), particularly when effective control strategies, including 238 vaccination are available. The potential for co-selection for resistance to cephalosporins in cattle is 239 well recognised and should increase concern regarding the unnecessary and overuse of tetracyclines 240 (Kanwar et al., 2014). The routine monitoring of calf serum total proteins and colostrum quality will 241 enable the early detection and subsequent investigation of issues within the colostrum management 242 process, and bacteriological analysis of colostrum may also be of interest if hygiene failures are 243 suspected. There is great potential for the veterinarian to have significant impact on calf health by 244 improving management factors such as colostrum management, which will lead to measurable 245 improvements in calf health and consequently reductions in AMU.

246 Infectious disease

247 Infectious disease control has been a significant part of veterinary surgeon led herd health planning 248 over many years. The drivers for infectious disease control include reducing disease (production, 249 economic and welfare impacts) and increasing stock value (trade). Key single agent infectious 250 diseases important in dairy herds include BVD, Bovine herpes virus (BHV), Leptospirosis, Johnes 251 Disease and Bovine Tuberculosis (bTB). BVD exacerbates calf disease through immunosuppression 252 (Lanyon et al., 2014), and BHV can cause pneumonia (IBR) and abortions (Graham 2013), and whilst 253 both BVD and BHV are viral infections, it is likely that AMU will increase in the face of disease. 254 Johne's Disease is bacterial in origin but considered untreatable, again increased AMU seems likely 255 due to the increased risk of other diseases (Tiwari et al., 2006). Bovine TB has the potential to 256 indirectly increase AMU through restrictions on livestock sales, resulting in overstocking of calves, or 257 restocking through purchases increasing infectious disease risk. 258 A number of disease control and eradication strategies and schemes are available, and it is plausible 259 that good control of single agent infectious diseases are not only good for health and productivity 260 but are also likely to lead to reductions in AMU. Regular bulk tank milk serological screening and the 261 adoption of appropriate biosecurity and/or vaccination strategies are commonly advocated for BVD, 262 IBR and Leptospirosis, although all approaches have their limitations. BVD eradication is supported by legislation in Scotland and industry led schemes in England (BVD Free) and Wales (Gwaredu BVD). 263 264 Johne's disease control requires control plan compliance over a sustained period of time, with 265 advice available from the National Action Group on Johne's (actionjohnesuk.org). Bovine TB control is achieved through statutory controls, and accreditation schemes (such as CHeCS) also exist and 266 267 again biosecurity is essential in control.

268 Retailers and milk buyers

269 Milk price banding has been used to pay for milk constituents for many years, and to incentivise
270 somatic cell count control since 1994. The milk price received and contractual relationship now

271 extends much more widely to cover AMU and herd health through aligned retailer contracts, which 272 create a direct relationship between retailer and supplier. These aligned contracts give the retailer 273 direct influence in the supply chain, allowing the retailer an opportunity to address issues such as 274 health, welfare and medicine residues, with the aim of building consumer trust. Contracts require 275 dairy farms to meet minimum standards and higher standards can be incentivised. Two methods of 276 AMU data collection exist – reporting directly by farmers, or reporting of antimicrobial sales by the 277 veterinary practice. Whichever collection method is used, benchmarking identifies AMU by type and 278 class.

279 AMU reporting can be used to influence antimicrobial selection, with retailers restricting access to 280 highest priority critically important antimicrobials, and this approach has been adopted from June 281 2018 by the Red Tractor Assurance Scheme. Treatment decision making is influenced through the 282 encouragement of selective dry cow therapy, which requires somatic cell count recording and 283 control. Farms with relatively high use of therapeutic antimicrobials can be identified as benefit is 284 likely to be seen from both improved disease control as well as implementing rational treatment 285 protocols if they do not yet exist. Benefits from an AMU reduction plan should be accrued by the 286 retailer (less reputation risk), the processor (less residue risk), the farmer (less cost), the cow (less 287 disease) and the veterinarian (herd health opportunities). Aligned contracts encourage farmer 288 engagement through benchmarking and incentives (potential for price or volume bonuses from high 289 performance) and risk (contracts may be lost from underperformance). While retailer contracts are 290 driving change and AMU reduction, this change should be beneficial to all, and is simply another step 291 towards increased preventive health.

292 Summary

The responsible use of antimicrobials on dairy farms is an important issue. By monitoring AMU and applying the principles of herd health to reducing disease associated with high AMU, significant decreases in AMU can be achieved. Reductions in AMU achieved by reducing disease are likely to be

- sustainable as well as good for animal welfare, farm profitability and production, whilst limiting the
- 297 dissemination of antimicrobials into the environment, not to mention an excellent opportunity for
- veterinarians interested in providing a herd health consultancy service to their farm clients.
- 299 Veterinarians have a great role to play in the training of farmers, and are clearly gatekeepers in AMU
- 300 prescription with an obligation to be in control of what is being prescribed to farms. Benchmarking
- 301 at practice level is an easy and effective method of identifying high usage farms and allows effective
- 302 AMU reductions to be rapidly achieved through targeted herd health interventions. Freely
- 303 downloadable tools are available both to measure and benchmark AMU on farms, and should
- 304 feature as a routine component of a herd health review, enabling veterinarians to engage with high
- 305 use farms, and reduce AMU by reducing disease incidence through proactive herd health
- 306 interventions.

307 Figures



308

309 Figure 1 A diagram illustrating high antimicrobial use on an example dairy farm





313 calculator (available to download for free from <u>www.dairy.ahdb.org.uk/technical-</u>

- 314 <u>information/animal-health-welfare/amu-calculator</u>) and Benchmarking tool (available to download
- 315 for free from <u>www.dairy.ahdb.org.uk/resources-library/technical-information/health-welfare/amu-</u>
- 316 <u>benchmarking-tool</u>) to assess AMU on the example farm (figure 1), and benchmark against other
- 317 farms



319 Figure 3 A diagram illustrating the scale of antimicrobial use reduction that could be achieved in the

320 example herd (Figure 1) by implementing the advice in the article

321 References

- ARCHER, S., BELL, N. & HUXLEY, J. (2010) Lameness in UK dairy cows: a review of the current status.
- 323 In Practice 32, 492-504
- 324 BARD, A. M., MAIN, D. C. J., HAASE, A. M., WHAY, H. R., ROE, E. J., & REYHER, K. K. (2017). The future
- 325 of veterinary communication: Partnership or persuasion? A qualitative investigation of veterinary
- 326 communication in the pursuit of client behaviour change. *PLOS ONE*, *12*(3)
- 327 BELL, N. J. (2017) Moving on from antibiotic foot baths for the control of digital dermatitis.
- 328 Veterinary Record 181, 51-51
- BELL, N. J., POTTERTON, S., BLOWEY, R., WHAY, H. R. & HUXLEY, J. N. (2014) Disinfectant
- 330 footbathing agents for the control of bovine digital dermatitis in dairy cattle. Livestock 19, 6-13
- BRADLEY, A., BREEN, J., LEACH, K., GIBBONS, J., ARMSTRONG, D. & GREEN, M. (2017) AHDB Dairy
 Mastitis Control Plan. Veterinary Record 180, 154-155
- BRADLEY, A. J. (2002) Bovine Mastitis: An Evolving Disease. The Veterinary Journal 164, 116-128
- BRADLEY, A. J., BREEN, J. E., PAYNE, B., WILLIAMS, P. & GREEN, M. J. (2010) The use of a
- cephalonium containing dry cow therapy and an internal teat sealant, both alone and in
- 336 combination. J Dairy Sci 93, 1566-1577
- 337 BREEN, J.E, JONES, B., JONES, N., JONES, M., EDWARDS, R., (2017) Implementation of the
- 338 AHDB dairy mastitis control plan to reduce clinical mastitis rate and antibiotic use in a large dairy
- herd. Proceedings of the British Mastitis Conference (2017) p 31- 42
- 340 CONSTABLE, P. D. (2004) Antimicrobial use in the treatment of calf diarrhea. Journal of veterinary341 internal medicine 18, 8-17
- 342 COOK, N. B. & NORDLUND, K. V. (2004) Behavioral needs of the transition cow and considerations
- 343 for special needs facility design. Vet Clin North Am Food Anim Pract 20, 495-520
- 344 DE SUTTER, A. I., DE MEYERE, M. J., DE MAESENEER, J. M. & PEERSMAN, W. P. (2001) Antibiotic
- prescribing in acute infections of the nose or sinuses: a matter of personal habit? Fam Pract 18, 209-213
- 347 DOWN, P. M., BRADLEY, A. J., BREEN, J. E. & GREEN, M. J. (2017) Factors affecting the cost-
- effectiveness of on-farm culture prior to the treatment of clinical mastitis in dairy cows. Preventive
 Veterinary Medicine 145, 91-99
- 350 DRILLICH, M., REICHERT, U., MAHLSTEDT, M. & HEUWIESER, W. (2006) Comparison of two strategies
- 351 for systemic antibiotic treatment of dairy cows with retained fetal membranes: preventive vs.
- 352 selective treatment. J Dairy Sci 89, 1502-1508
- EVANS, N. J., MURRAY, R. D. & CARTER, S. D. (2016) Bovine digital dermatitis: Current concepts from
 laboratory to farm. The Veterinary Journal 211, 3-13
- 355 GILBERT, R. O. (2016) Management of Reproductive Disease in Dairy Cows. Veterinary Clinics of
- 356 North America: Food Animal Practice 32, 387-410
- 357 GORDEN, P. J. & PLUMMER, P. (2010) Control, Management, and Prevention of Bovine Respiratory
- Disease in Dairy Calves and Cows. Veterinary Clinics of North America: Food Animal Practice 26, 243 259
- 360 GRAHAM, D. A. (2013) Bovine herpes virus-1 (BoHV-1) in cattle-a review with emphasis on
- 361 reproductive impacts and the emergence of infection in Ireland and the United Kingdom. Irish
- 362 Veterinary Journal 66, 15-15
- 363 GREEN, M. J. (2012) Dairy herd health, CABI
- 364 GREEN, M. J., LEACH, K. A., BREEN, J. E., GREEN, L. E. & BRADLEY, A. J. (2007) National intervention
- 365 study of mastitis control in dairy herds in England and Wales. Vet Rec 160, 287-293
- 366 GROENEVELT, M., MAIN, D. C. J., TISDALL, D., KNOWLES, T. G. & BELL, N. J. (2014) Measuring the
- 367 response to therapeutic foot trimming in dairy cows with fortnightly lameness scoring. The
- 368 Veterinary Journal 201, 283-288
- 369 HAIMERL, P., HEUWIESER, W., & ARLT, S. (2013). Therapy of bovine endometritis with prostaglandin
- 370 F2α: A meta-analysis. *Journal of Dairy Science*, *96*(5), 2973–2987
- HOBMAN, J. L., & CROSSMAN, L. C. (2018). Bacterial antimicrobial metal ion resistance.

- HYDE, R. M., REMNANT, J. G., BRADLEY, A. J., BREEN, J. E., HUDSON, C. D., DAVIES, P. L., CLARKE, T.,
- 373 CRITCHELL, Y., HYLANDS, M., LINTON, E., WOOD, E. & GREEN, M. J. (2017) Quantitative analysis of
 374 antimicrobial use on British dairy farms. Veterinary Record 181, 683-683
- HYDE, B., & BRENNAN, M. (2017). BestBETs for Vets. *The Veterinary Record*, 180(15), 380–381.
- HYDE, R., GREEN, M., REMNANT, J., DOWN, P., HUXLEY, J., DAVIES, P., ... BREEN, J. (2017). Tool to
 measure antimicrobial use on farms. *The Veterinary Record*, *180*(7), 183
- 378 JONES, P. J., MARIER, E. A., TRANTER, R. B., WU, G., WATSON, E. & TEALE, C. J. (2015) Factors
- 379 affecting dairy farmers' attitudes towards antimicrobial medicine usage in cattle in England and
- 380 Wales. Preventive Veterinary Medicine 121, 30-40
- 381 KANWAR, N., SCOTT, H. M., NORBY, B., LONERAGAN, G. H., VINASCO, J., COTTELL, J. L., CHALMERS,
- 382 G., CHENGAPPA, M. M., BAI, J. & BOERLIN, P. (2014) Impact of treatment strategies on
- 383 cephalosporin and tetracycline resistance gene quantities in the bovine fecal metagenome. Sci Rep384 4, 5100
- 385 KROMKER, V. & LEIMBACH, S. (2017) Mastitis treatment-Reduction in antibiotic usage in dairy cows.
 386 Reprod Domest Anim 52 Suppl 3, 21-29
- 387 KUIPERS, A., KOOPS, W. J. & WEMMENHOVE, H. (2016) Antibiotic use in dairy herds in the
- 388 Netherlands from 2005 to 2012. J Dairy Sci 99, 1632-1648
- 389 LAGO, A., GODDEN, S. M., BEY, R., RUEGG, P. L., & LESLIE, K. (2011). The selective treatment of
- 390 clinical mastitis based on on-farm culture results: I. Effects on antibiotic use, milk withholding time,
- and short-term clinical and bacteriological outcomes. Journal of Dairy Science, 94(9), 4441–4456
- LANYON, S. R., HILL, F. I., REICHEL, M. P. & BROWNLIE, J. (2014) Bovine viral diarrhoea: pathogenesis
 and diagnosis. Vet J 199, 201-209
- LAVEN, R. A. & LOGUE, D. N. (2006) Treatment strategies for digital dermatitis for the UK. The
 Veterinary Journal 171, 79-88
- LEACH, K. A., TISDALL, D. A., BELL, N. J., MAIN, D. C. J. & GREEN, L. E. (2012) The effects of early
- treatment for hindlimb lameness in dairy cows on four commercial UK farms. The Veterinary Journal193, 626-632
- LESLIE, K. E. & PETERSSON-WOLFE, C. S. (2012) Assessment and management of pain in dairy cows
 with clinical mastitis. Vet Clin North Am Food Anim Pract 28, 289-305
- 401 LORENZ, I., MEE, J. F., EARLEY, B. & MORE, S. J. (2011) Calf health from birth to weaning. I. General 402 aspects of disease prevention. Irish Veterinary Journal 64, 10-10
- 403 MAXWELL, O., MIGUEL-PACHECO, G., NEWSOME, R., RANDALL, L., REMNANT, J., THOMAS, H. &
- 404 HUXLEY, J. (2015) Lameness in cattle 1. Recent research to inform clinical practice. In Practice 37, 405 127-138
- 406 MEGANCK, V., HOFLACK, G. & OPSOMER, G. (2014) Advances in prevention and therapy of neonatal
- 407 dairy calf diarrhoea: a systematical review with emphasis on colostrum management and fluid
 408 therapy. Acta Veterinaria Scandinavica 56, 75
- 409 MILLS, H. L., TURNER, A., MORGANS, L., MASSEY, J., SCHUBERT, H., REES, G., BARRETT, D., DOWSEY,
- 410 A. & REYHER, K. K. (2018) Evaluation of metrics for benchmarking antimicrobial use in the UK dairy
- 411 industry. Veterinary Record 182, 379-379
- 412 NEWSOME, R., GREEN, M. J., BELL, N. J., CHAGUNDA, M. G. G., MASON, C. S., RUTLAND, C. S.,
- 413 STURROCK, C. J., WHAY, H. R. & HUXLEY, J. N. (2016) Linking bone development on the caudal
- 414 aspect of the distal phalanx with lameness during life. Journal of Dairy Science 99, 4512-4525
- 415 O'NEILL, J. (2015) Antimicrobials in agriculture and the environment: reducing unnecessary use and
- 416 waste the review on antimicrobial resistance. In Review on antimicrobial resistance
- 417 OSPINA, P. A., MCART, J. A., OVERTON, T. R., STOKOL, T. & NYDAM, D. V. (2013) Using nonesterified
- 418 fatty acids and beta-hydroxybutyrate concentrations during the transition period for herd-level
- 419 monitoring of increased risk of disease and decreased reproductive and milking performance. Vet
- 420 Clin North Am Food Anim Pract 29, 387-412

- 421 RICCI, A., ALLENDE, A., BOLTON, D., CHEMALY, M., DAVIES, R., FERNÁNDEZ ESCÁMEZ, P. S., ...
- 422 HERMAN, L. (2017). Risk for the development of Antimicrobial Resistance (AMR) due to feeding of 423 calves with milk containing residues of antibiotics. *EFSA Journal*, *15*(1).
- 424 RUIZ, R., TEDESCHI, L. O., & SEPÚLVEDA, A. (2017). Investigation of the effect of pegbovigrastim on
- some periparturient immune disorders and performance in Mexican dairy herds. Journal of Dairy
- 426 Science, 100(4), 3305–3317
- 427 RUMA (2017) Targets Task Force Report 2017
- 428 SAINI, V., MCCLURE, J. T., SCHOLL, D. T., DEVRIES, T. J. & BARKEMA, H. W. (2013) Herd-level
- 429 relationship between antimicrobial use and presence or absence of antimicrobial resistance in gram-
- 430 negative bovine mastitis pathogens on Canadian dairy farms. J Dairy Sci 96, 4965-4976
- 431 SAWANT, A. A., SORDILLO, L. M. & JAYARAO, B. M. (2005) A survey on antibiotic usage in dairy herds 432 in Pennsylvania. J Dairy Sci 88, 2991-2999
- 433 SHERWIN, G. & DOWN, P. (2018) Calf immunology and the role of vaccinations in dairy calves. In 434 Practice 40, 102-114
- 435 SPEKSNIJDER, D. C., MEVIUS, D. J., BRUSCHKE, C. J. & WAGENAAR, J. A. (2015) Reduction of
- 436 veterinary antimicrobial use in the Netherlands. The Dutch success model. Zoonoses Public Health
- 437 62 Suppl 1, 79-87
- 438 TANG, K. L., CAFFREY, N. P., NÓBREGA, D. B., CORK, S. C., RONKSLEY, P. E., BARKEMA, H. W.,
- 439 POLACHEK, A. J., GANSHORN, H., SHARMA, N., KELLNER, J. D. & GHALI, W. A. (2017) Restricting the
- 440 use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-
- 441 producing animals and human beings: a systematic review and meta-analysis. The Lancet Planetary
 442 Health 1, e316-e327
- 443 THOMAS, H. J., MIGUEL-PACHECO, G. G., BOLLARD, N. J., ARCHER, S. C., BELL, N. J., MASON, C.,
- 444 MAXWELL, O. J. R., REMNANT, J. G., SLEEMAN, P., WHAY, H. R. & HUXLEY, J. N. (2015) Evaluation of
- treatments for claw horn lesions in dairy cows in a randomized controlled trial. Journal of DairyScience 98, 4477-4486
- 447 THOMAS, H. J., REMNANT, J. G., BOLLARD, N. J., BURROWS, A., WHAY, H. R., BELL, N. J., MASON, C. &
- HUXLEY, J. N. (2016) Recovery of chronically lame dairy cows following treatment for claw horn
 lesions: a randomised controlled trial. Veterinary Record 178, 116-116
- 450 TISDALL, D. A., REYHER, K. K. & BARRETT, D. C. (2016) Developing a multifaceted, collaborative,
- 451 practice-wide approach to responsible medicines use on farms. Proceedings of World Buiatrics

452 Congress 2016, 129-130

- 453 TIWARI, A., VANLEEUWEN, J. A., MCKENNA, S. L. B., KEEFE, G. P. & BARKEMA, H. W. (2006) Johne's
- disease in Canada: Part I: Clinical symptoms, pathophysiology, diagnosis, and prevalence in dairy
 herds. The Canadian Veterinary Journal 47, 874-882
- 456 TURNER, A., TISDALL, D., BARRETT, D. C., WOOD, S., DOWSEY, A. & REYHER, K. K. (2018) Ceasing the
- use of the highest priority critically important antimicrobials does not adversely affect production,health or welfare parameters in dairy cows. Veterinary Record
- 459 VAN DIJK, L., HAYTON, A., MAIN, D. C. J., BOOTH, A., KING, A., BARRETT, D. C., ... REYHER, K. K.
- 460 (2017). Participatory Policy Making by Dairy Producers to Reduce Anti-Microbial use on Farms.
- 461 *Zoonoses and Public Health*, *64*(6), 476–484
- VMD. (2013). VMD revises advice on chlortetracyline use in calf milk replacer. *The Veterinary Record*,
 172(3), 58
- 464 WENZ, J. R., GARRY, F. B., LOMBARD, J. E., ELIA, R., PRENTICE, D. & DINSMORE, R. P. (2005) Short
- 465 communication: Efficacy of parenteral ceftiofur for treatment of systemically mild clinical mastitis in
 466 dairy cattle. J Dairy Sci 88, 3496-3499
- 467 ZINICOLA, M., KORZEC, H., TEIXEIRA, A. G. V., GANDA, E. K., BRINGHENTI, L., TOMAZI, A. C. C. H., ...
- 468 BICALHO, R. C. (2018). Effects of pegbovigrastim administration on periparturient diseases, milk
- 469 production, and reproductive performance of Holstein cows. Journal of Dairy Science
- 470